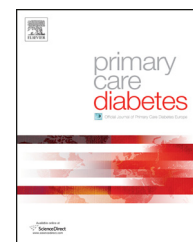




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## Original research

# Increasing trend in emergency department visits for hypoglycemia from patients with type 2 diabetes mellitus in Taiwan



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## ABSTRACT

**Aims:** We analyze the time trends of hypoglycemia-related emergency department visits in Taiwan between 2000 and 2010, focusing on type 2 diabetic patients receiving antidiabetic agents.

**Methods:** From a national dataset containing longitudinal medical claims of one million persons, we ascertained 4479 hypoglycemia-related emergency department visits from 3184 type 2 diabetic patients for analysis. We used negative binomial regression to calculate the incidence rate ratios (IRRs) for comparing event rates of hypoglycemia-related emergency department visits in different study periods.

**Results:** Rates of hypoglycemia-related emergency department visits increased 4.8 folds from year 2000 to 2010 (adjusted IRR 4.88, 95% CI 3.94–6.05,  $P < 0.001$ ). Severe hypoglycemia requiring emergency department visits prevailed among women, older patients ( $\geq 65$  years), and those not lived in the urban areas.

**Conclusions:** Within a 10-year period, there was a substantial increase in the rates of hypoglycemia-related emergency department visits from type 2 diabetic patients in Taiwan. Appropriate risk management plans should be developed to prevent the occurrence of severe hypoglycemia in patients with type 2 diabetes in Taiwan.

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## 1. Introduction

Hypoglycemia, an often underappreciated problem, is the most common and serious side effect of glucose-lowering therapy in patients with diabetes mellitus [1]. An hypoglycemic event requiring assistance of another person for recovery is defined as severe hypoglycemia [2]. Iatrogenic hypoglycemia is the most frequent cause of severe hypoglycemic attack [3]. Evidence has shown that patients with type 2 diabetes might be particularly vulnerable to acute and long-term adverse outcomes associated with severe hypoglycemia [4–6]. Published event rates for severe iatrogenic hypoglycemia in type 2 diabetes vary from 0.03 to 0.73 episodes per patient per year [7], depending on the methods of data collection, the patients included, and the definition of hypoglycemia. It is a challenge to estimate the frequency of and risk factors for severe hypoglycemia, especially in a national scope, in patients with type 2 diabetes because ascertainment of this severe condition is often incomplete [8] and glycemic thresholds for symptoms of hypoglycemia shift from one patient to another [2].

Emergency department (ED) visit for hypoglycemia may serve as a reliable epidemiological marker of severe hypoglycemia because it is dramatic, requiring assistance of another person, and easily captured by medical claims database. It has been reported that about 1.2 million ED visits between 2006 and 2009 were attributable to hypoglycemia in the United State [9]. Ginde et al. reported that approximately 25% patients who visited ED for hypoglycemia required hospital admission [10]. In addition, Parsaik et al. recently reported that 34% of the type 2 diabetic patients with severe hypoglycemia requiring emergency medical service died within 3 years of their first event [11]. These results highlight the need of additional studies to explore the epidemiology of hypoglycemia-related ED visits from patients with type 2 diabetes.

In this study, we focus on type 2 diabetic patients receiving antidiabetic agents and report the national trends in ED visits for hypoglycemia from these patients. The impacts of demographic factors such as age, sex and level of urbanization on the incidence of ED visits for hypoglycemia are also characterized in the study.

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## 2. Methods

### 2.1. Study population

The National Health Insurance Program is a state-run dominant healthcare payer in Taiwan, covering 23 million beneficiaries (almost 99.5% of the Taiwanese population). A research database, the National Health Insurance Research Database (NHIRD), is derived from the National Health Insurance claims data and it provides comprehensive information on patients' demography, disease diagnosis, and prescription details to researchers. Several dozens of sampled datasets extracted from the NHIRD are available to researchers in Taiwan nowadays.

The dataset used in this study is the Longitudinal Health Insurance Dataset of the NHIRD, a representative dataset containing medical information of one million subjects randomly selected from all insured persons in the NHIRD in 2000. All medical records of the selected insurers from 2000 to 2010, including outpatient and ED visits, hospitalization, medication use, and diagnostic data (coded by the International Classification of Diseases, 9th Revision, Clinical Modification, ICD-9-CM), were included in the dataset. The original identification number was encrypted by using a double-scrambling protocol to protect privacy of the patient. However, each subject in the dataset kept the same serial number while the dataset provider maintains data integrity. This enables researchers to follow up an individual patient by linking new claims data belonging to the same patient within the NHIRD without knowing the original identification number of the patient. Our study protocol was approved by the Institutional Review Board of the Taipei Veterans General Hospital and was conducted in accordance with the Helsinki Declaration.

### 2.2. Study design

In the current study, we first identified severe hypoglycemic episodes requiring emergency treatment from year 2000 to 2010 in the Longitudinal Health Insurance Dataset. The hypoglycemic episodes were defined by searching all ED visits for a primary diagnosis of the following ICD-9-CM codes: 251.0 (hypoglycemic coma), 251.1 (other specified hypoglycemia) and 251.2 (hypoglycemia, unspecified). Then, we ascertained events from patients probably with type 2 diabetes among the entire hypoglycemia-associated ED visits. The diagnosis of type 2 diabetes was made by searching for A code of A181 and the following ICD-9-CM codes: 250.00, 250.0, 250.1, 250.2, 250.3, 250.4, 250.5, 250.6, 250.7, 250.8, 250.9, 250.02, 250.10, 250.20, 250.30, 250.40, 250.50, 250.60, 250.70, 250.80, 250.84, 250.90. Moreover, any patient with a diagnosis of type 2 diabetes should have at least three consecutive outpatient claims or one inpatient claims with the above-mentioned ICD-9-CM codes occurring in the year prior to the first hypoglycemia-related ED visit. We excluded the events from patients who might be cases of type 1 diabetes by searching the following ICD9-CM codes 250.01, 250.11, 250.21, 250.31, 250.51, 250.41, 250.61, 250.71, 250.81, and 250.91 and A code of A181A in the medical records one year before the hypoglycemic attacks. We also excluded the episodes from patients younger than 45 years old to avoid possible misclassification of type 1 diabetes as type 2 diabetes and excluded several episodes with missing data (mostly gender information). Finally, we included events from patients who received at least one oral hypoglycemic agent (with or without concomitant use of insulin) in the 3 months prior to the ED visit or who used insulin therapy only for more than 7 days before the ED visit to ensure that the hypoglycemic events were from type 2 diabetic patients receiving antidiabetic agents. To avoid double counting of the same episode of hypoglycemia-related ED visit, we further excluded any hypoglycemic episodes that occurred within 3 days after a prior hypoglycemic event.

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